BrightFocus® Foundation | National Glaucoma Research

# Today's investments, tomorrow's breakthroughs.

## 2024 National Glaucoma Research Projects






National Glaucoma Research

# Meet the Next Generation of Innovators

An estimated 80 million people around the world have glaucoma, with 111 million projected to have it by 2040. In the United States, where the disease disproportionately affects and is a leading cause of blindness among African American and Latino communities, more than three million people live with glaucoma.

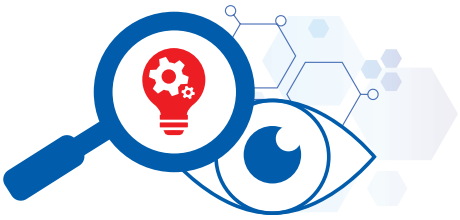
National Glaucoma Research, a BrightFocus Foundation program, is on a mission to cure this sight-stealing disease. We believe that by providing initial funding for highly innovative, experimental research and creative ideas, we can spark revolutionary approaches and vision-saving breakthroughs.

Explore all active grants:
**brightfocus.org/NGRgrants**

We're funding
**38**
active glaucoma research projects worldwide.

**Since inception:**
We've funded more than
**$51 million**
in research grants.

**Since inception:**
We've supported
**1,636**
scientists across 496 grants.



# Our 360-Degree Approach

We take a 360-degree approach to funding innovative scientific research worldwide to defeat glaucoma. As you'll see in the pages that follow, our funded researchers are exploring the full range of scientific paths toward a better understanding of the root causes of the disease, prevention strategies, treatments, and ultimately a cure for glaucoma.

This research portfolio provides an overview of our current National Glaucoma Research grant projects. Grants are vetted through a rigorous evaluation process by the world's top scientists and clinicians who serve on our Scientific Review Committee.

We are deeply grateful to our donors, whose generosity empowers the next generation of researchers to pursue innovative, bold, and promising science, bringing us closer to tomorrow's cure.

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*This portfolio reflects awarded grants as of July 3, 2024.*

# Controlling Eye Pressure in New Ways

Elevated intraocular pressure (IOP) is common in glaucoma when the aqueous humor cannot drain properly. Normally, this fluid drains through the trabecular meshwork into Schlemm's canal and into the bloodstream. Blockages, increased fluid volume, and trabecular meshwork stiffness can raise eye pressure. Grantees are investigating ways to regulate eye pressure, reduce stiffness, and control IOP.

## The Role of Podosomes in Regulating Eye Pressure

**Michael G. Anderson, PhD** | University of Iowa

For this project, researchers will test the role of podosomes, small fingerlike protrusions of cells, and their effect on eye pressure. This work will lead to important information about the cell biology of glaucoma, including possibly identifying the precise molecular location of outflow resistance. The findings also may point to compounds altering podosomes as potential new glaucoma therapies.

## Next-Generation Glaucoma Drugs to Selectively Release the Pressure-Building Block in Schlemm's Canal*

**C. Ross Ethier, PhD** | Georgia Institute of Technology

Endothelial cells of the inner wall of Schlemm's canal (SC) play a key role in homeostatic control mechanisms that maintain intraocular pressure (IOP) within a target range. The long-term goal of this project is to develop novel therapies that directly target SC cells to improve IOP control. These targeted therapies will be highly effective because of their specificity and thus greatly benefit glaucoma patients.

**Part of a joint research award for a collaborative interinstitutional grant.*

## The Study of Segmental Aqueous Outflow in Uveal Drainage Pathway

**Haiyan Gong, MD, PhD** | Boston University
*Co-Principal Investigator: Carol Toris, PhD, University of Nebraska Medical Center*

Uveal outflow, one of two routes for fluid drainage from the eye, plays a role in maintaining normal pressure inside the eye (IOP). Prostaglandin analogue drugs lower increased IOP in glaucoma by enhancing uveal outflow. This group recently found that uveal outflow is segmental, or nonuniform, around the eye, although the regulating factors involved are unclear. The researchers will further investigate segmental uveal outflow and the factors that may regulate it.

## How the Microenvironment Affects Schlemm's Canal Cell Behavior

**Samuel Herberg, PhD** | SUNY Upstate Medical University

Glaucoma is a leading cause of blindness worldwide, but exactly what causes the disease is unclear. Using a first-of-its-kind 3D fluid drainage tissue model system, the researchers seek to investigate the contributions of glaucomatous biomechanical cues in driving Schlemm's canal cell mechano-dysfunction. This work will set the stage for the identification of future glaucoma therapies targeting cellular biomechanics.

## A Novel Gene-Therapy Approach for Glaucoma*

**Simon John, PhD** | Columbia University
*Co-Principal Investigator: Krish Kizhatil, PhD, The Jackson Laboratory*

Researchers will develop and test resources for Schlemm's canal-specific targeting and expression of genes for gene therapy. Successful development of this targeted therapy will help control eye pressure more effectively and provide better glaucoma treatment options.

## The Role of Microtubules in Glaucomatous Schlemm's Canal Mechanobiology

**Haiyan Li, PhD** | Georgia Institute of Technology
*Mentor: C. Ross Ethier, PhD*

Intraocular pressure is largely controlled by tissues at or near the Schlemm's canal inner wall endothelium, where reduced fluid conductivity occurs in glaucoma. This project aims to investigate the impact of microtubules, crucial components of the cytoskeleton, on Schlemm's canal cell mechanobiology and intraocular pressure, a key risk factor for glaucoma.

## IOP-Related Gene Responses in the Optic Nerve Head and Trabecular Meshwork

**Diana C. Lozano, PhD** | Oregon Health & Science University
*Co-Principal Investigator: Kate Keller, PhD*

Elevated intraocular pressure (IOP) is a leading risk factor for primary open-angle glaucoma. Yet, the cellular events that comprise protective homeostatic IOP responses, or damaging events leading to tissue injury, are poorly understood. Researchers will investigate how mild and repeat IOP elevations modify the molecular mechanisms in ocular tissues implicated in glaucoma pathogenesis. This study will advance understanding how subtle IOP exposures can cumulatively develop into chronic glaucoma.

## An Effective Tool for Understanding Dysfunctional Eye Drainage in Glaucoma

**Weiming Mao, PhD** | Indiana University

For this project, researchers will develop a mouse model of eye drainage dysfunction in glaucoma that will allow for more straightforward investigations of how fluid buildup occurs. The tool is expected to support scientists in better understanding how glaucoma develops and offer a way to test candidate treatments.

## Building a Better Model to Screen for Intraocular Pressure-Lowering Glaucoma Drugs

**Darryl Overby, PhD** | Imperial College London (UK)

Researchers will assess Schlemm's canal cells, which modulate fluid drainage from the eye, for their role in the fluid buildup of glaucoma. The team will recreate the natural environment of these cells to test how they form a barrier to fluid outflow and to test candidate treatments. The model is expected to support faster evaluation and transition of candidate drugs to clinical testing for glaucoma.

## Developing New Drugs to Lower Eye Pressure in Glaucoma*

**Darryl Overby, PhD** | Imperial College London (UK)
*Co-Principal Investigator: Joseph M. Sherwood, PhD*

This group has identified a particular cell type (Schlemm's canal cells) that regulates eye pressure by controlling the drainage of aqueous humor from the eye. They will develop and apply novel screening technologies to identify new drugs to lower eye pressure by improving aqueous humor drainage across Schlemm's canal cells.

**Part of a joint research award for a collaborative interinstitutional grant.*

### Long-Lasting, Nonsurgical Treatment for Eye Pressure in Glaucoma

**Mark Prausnitz, PhD** | Georgia Institute of Technology

The aim of this project is to test the safety and efficacy of an expanding gel to relieve fluid buildup in the eye in glaucoma. The injectable gel could offer a nonsurgical, nondrug treatment of eye pressure in glaucoma that could last months. Success will set the stage to move into clinical trials.

### Next-Generation Glaucoma Drug Development*

**W. Daniel Stamer, PhD** | Duke University

For this project, researchers will screen candidate molecular biology tools that could be used to target drugs to different eye structures affected by glaucoma. The eye structures are the trabecular network, which controls fluid drainage from the eye, and Schlemm's canal, where draining fluid passes to the circulatory system. Fine-tuning ways to target each of these separately could open new paths to drug development in glaucoma.

# Imaging & Exploring the Eye-Brain Connection

Glaucoma causes tiny blind spots, or visual field defects, that can lead to vision loss and blindness, with progression varying among individuals. Early diagnosis is key, and advances in eye imaging now detect the tiniest changes preceding glaucoma. National Glaucoma Research grant recipients are developing new technologies to image retinal ganglion cells and are investigating cellular communication disruptions, aiming for earlier detection of the disease and new treatments.

### Improved Imaging of the Outflow Pathway in the Living Human Eye

**Alessandra Carmichael-Martins, PhD** | University of Bonn (Germany)
*Mentor: Stephen Burns, PhD, Indiana University, Bloomington*

This work is expected to enable researchers and clinicians to achieve 3-dimensional images of the drainage structures in the living human eye at cellular-level resolution. This tool will facilitate a deeper understanding

of changes within the trabecular meshwork associated with age, glaucoma, and treatment.

### The Impact of Glaucoma on Light-Mediated Mood and Sleep Disorders

**Xiaorong Liu, PhD** | University of Virginia
*Co-Principal Investigator: Ignacio Provencio, PhD*

A subset of retinal ganglion cells (RGCs), known as ipRGCs, transmit light information from the eyes to the brain for purposes beyond vision, such as regulating sleep and mood. Because glaucoma patients often suffer from light-induced sleep and mood disturbances, researchers aim to understand how ipRGCs control light's effects on mood and sleep.

### Increased Eye Pressure Affects the Neuronal Communications in the Brain

**Prabhavathi Maddineni, PhD** | University of North Texas Health Science Center
*Mentor: Gulab Zode, PhD*

The optic nerve is part of the central nervous system and is connected to the brain, and pressure-induced optic nerve damage may also damage surrounding cells and neurons in the brain. The aim of this study is to ascertain how neurons in the brain communicate with each other in response to this pressure-induced damage.

# Predicting Outcomes & Other Treatment Innovations

Approved glaucoma treatments mainly focus on lowering eye pressure through eye drops or surgery, but these require consistency and carry risks. More reliable treatments addressing the underlying causes beyond eye pressure are needed. Grant recipients are developing drugs to lower eye pressure and protect nerve cells and exploring genome-editing approaches to restore trabecular meshwork function, stem cell transplantation, lifestyle interventions, and strategies to communicate genetic testing with at-risk individuals.

## Saving Sight: A Journey to Healing Without Scars

**Jennifer Fan Gaskin, MBChB, MD, FRANZCO** | Centre for Eye Research Australia (Australia)
*Co-Principal Investigators: Elsa Chan, PhD & Roy Kong, PhD*

Minimally invasive glaucoma surgery is an increasingly popular treatment to prevent ongoing vision loss from glaucoma. However, its success is limited by scarring, and the current use of antiscarring cancer drugs carry serious long-term risks. This project aims to develop a more effective and safer alternative to improve long-term success of glaucoma surgery and to improve the quality of life for glaucoma patients worldwide.

## Can Regular Exercise Slow Glaucoma Progression?

**András Komáromy, DVM, PhD** | Michigan State University

Using models of naturally occurring glaucoma, researchers will determine if regular, moderate-intensity exercise can slow glaucoma disease progression. They also plan to evaluate metabolic biomarkers of exercise-induced neuroprotection in this model. If results are positive, exercise would represent an easy, low-cost, beneficial therapy avenue for glaucoma patients.

## An Optimal Form of Nerve Growth Factor as a New Neuroprotective Drug for Glaucoma

**Silvia Marinelli, PhD** | European Brain Research Institute (Italy)
*Co-Principal Investigator: Francesca Malerba, PhD*

For this project, researchers will dial down the negative effects of a naturally occurring molecule and boost its potential benefits as a glaucoma treatment. The optimized version of a "painless nerve growth factor" is expected to rescue retinal ganglion cells from progressive damage. The drug is already in clinical trials for other eye diseases.

## Retinal Ganglion Cell Axon Degeneration in a 3D Microfluidic Hydrogel Model

**Shruti Patil, PhD** | Indiana University
*Mentor: Jason Meyer, PhD*

Retinal ganglion cell (RGC) axons traversing the optic nerve head are highly susceptible to glaucomatous damage, yet the link between optic nerve head biomechanics and RGC axonal degeneration remains poorly understood. To address this, researchers will implement 3D platforms integrating microfluidics and hydrogels with tunable stiffness to model biomechanical aspects affecting RGC axons in the optic nerve head. This offers hope for more effective glaucoma treatments.

## Using Laser Pulses to Smooth the Way for Transplanted Retinal Ganglion Cells in Glaucoma

**Karen Peynshaert, PhD** | Ghent University (Belgium)
*Mentor: Katrien Remaut, PhD*

Investigators will pilot the use of laser pulse technology to facilitate successful transplant of donor retinal ganglion cells in glaucoma. They will combine laser pulses with a heat-absorbing dye to make the smallest opening possible in the eye membrane to allow passage of transplanted cells. If successful, the method will offer a controlled, targeted way to create this passage for cells while causing the least disruption to important structures of the eye.

## Cell-to-Cell Communication in Health and Disease

**Michael Risner, PhD** | Oakland University William Beaumont School of Medicine
*Co-Principal Investigator: David Calkins, PhD, Vanderbilt University*

Using high-resolution microscopy, researchers will track the movement of mitochondria between cells through tubes connecting different cell types. The team is exploring possible backup pathways that may activate when stress interferes with this mitochondrial transfer. The findings will add to our understanding of the metabolic interaction between healthy and stressed cells in the context of cell transplantation for the treatment of glaucoma.

## Investigating Autophagy in Nitric Oxide Production to Control Eye Pressure

**Myoungsup Sim, PhD** | Duke University School of Medicine

Several studies have shown that nitric oxide (NO) lowers eye pressure. However, most of the NO-based drugs have failed to be approved by the Food and Drug Administration due to challenges related to the delivery of NO, suggesting that regulation of the cells' own NO production could represent a better strategy for glaucoma treatment. Researchers will investigate how to regulate endogenous NO production to improve the current NO-based glaucoma therapy.

## Developing Communication Strategies for Genetic Risk Testing in Glaucoma

**Emmanuelle Souzeau, PhD** | Flinders University of South Australia (Australia)
*Mentor: Jamie E. Craig, DPhil, FRANZCO*

Polygenic risk scores (PRS) for glaucoma make genetic testing an ideal strategy to identify at-risk individuals who can benefit from early management to reduce preventable blindness. However, the current lack in reporting strategies to efficiently communicate PRS to patients impedes the implementation of testing in clinical practice. Researchers aim to develop the first patient-friendly reports and assess delivery methods for risk communication of PRS for glaucoma, which will ultimately benefit at-risk individuals globally.

### Harnessing Artificial Intelligence to Improve Glaucoma Clinical Trials

**Jithin Yohannan, MD, MPH** | Johns Hopkins University School of Medicine

Researchers will deploy artificial intelligence to make glaucoma-related clinical trial enrollment and follow-up more efficient. Tools will be developed that can screen for patients who are a good fit for the repeated tests most trials entail and are at high risk for disease progression. The findings are expected to make clinical trials of new glaucoma therapies faster and less costly, translating into quicker assessment and approval of candidate treatments for glaucoma.

# Protecting & Regenerating the Optic Nerve

**Unlike most cells, the nerve cells providing vision don't regrow once damaged. National Glaucoma Research supports efforts to protect and regenerate retinal ganglion cells (RGCs), which carry visual signals from the eye to the brain. Researchers are also developing neuroprotective drugs to nourish and support fragile RGCs for long-term viability.**

### A Dietary Supplement in Treatment of Glaucoma

**Jeffrey Boatright, PhD** | Emory University
*Co-Principal Investigator: Ying Li, MD, PhD*

Mitochondria are the energy factories of cells. The mitochondria of retinal ganglion cells (RGCs) lose function with age, probably because of age-related loss of nicotinamide adenine dinucleotide (NAD+), an enzyme cofactor needed for energy production, making the cells more susceptible to damage. Researchers will test whether systemic delivery of the NAD+ precursor nicotinamide riboside, a dietary supplement, increases retinal NAD+ and protects RGCs in glaucoma models.

## Boosting Neuronal Energy to Improve Vision in Glaucoma

**Adriana Di Polo, PhD** | University of Montreal Hospital Center (Canada)

Researchers will test the effects of small molecules that can clear potentially damaging calcium buildup from retinal ganglion cells and keep the cells' mitochondria healthy and functioning efficiently. The small molecules are "mitochondrial uncouplers" because they uncouple mitochondrial processes that normally lead to production of damaging byproducts. If mitochondrial uncouplers show potential benefit, the project is expected to open the door to clinical trials of these drugs in glaucoma.

## Preserving the Eye's Vision by Neuroprotecting Retinal Cells

**Marco Feligioni, PhD** | European Brain Research Institute (Italy)

Neuroprotection is an unmet medical need. This project aims to investigate the properties of a new drug to protect against degeneration of retinal ganglion cells. Researchers will investigate the interaction of a pair of proteins previously implicated in damage to these cells. They will also use a mouse model to test whether a specific molecule they have identified can prevent these effects.

## Neuroprotection and Neuroenhancement in Glaucoma

**Jeffrey Goldberg, MD, PhD** | Stanford University

The goal of this project is to evaluate safety and proof of concept for whether ciliary neurotrophic factor can enhance vision or protect against vision loss in glaucoma. In this randomized trial, researchers will evaluate the retina and optic nerve in patients using a series of biomarkers to increase the chance of detecting evidence of vision improvement or protection against vision loss.

## Targeting Eye Immune Cells to Prevent Glaucoma-Induced Nerve Damage

**Shubham Maurya, PhD** | University of California, Berkeley
*Mentor: Karsten Gronert, PhD*

The aim of this project is to learn how microglia in the eye contribute to nerve damage in glaucoma and to test molecules that might prevent it. Researchers will work with naturally occurring small molecules that may dampen the reaction of the microglia. They also will sort out how astrocytes produce these small molecules and usually keep microglia in check, highlighting potential treatment targets in glaucoma.

## Repurposing an Approved Diabetes Drug for Glaucoma

**Kazuya Oikawa, PhD, BVSc** | University of Wisconsin-Madison
*Mentor: Gillian McLellan, BVMS, PhD, DECVO, DACVO, FARVO*

For this project, researchers will repurpose an FDA-approved diabetes drug as an anti-neuroinflammatory therapy for glaucoma. The drug mimics a naturally occurring insulin-regulating hormone and targets myeloid cells, which are implicated in neuroinflammation in glaucoma. The group expects to demonstrate that this already approved drug can be repurposed to target neuroinflammation in glaucoma.

## Mapping the Pathways of Neurodegeneration in Glaucoma Using Artificial Intelligence

**Karthik Shekhar, PhD** | University of California, Berkeley

Researchers will use innovative molecular techniques, artificial intelligence approaches, and mouse models to tease apart how different cell pathways interact in cell destruction in glaucoma. Focusing on the death of retinal ganglion cells, which underlies vision loss in the disease, the team will create a detailed molecular map of how and where neurodegeneration occurs in these cells, opening the way to new treatment possibilities and use of these tools in human studies.

## Pressure-Induced Axon Damage and Its Link to Glaucoma-Related Vision Loss

**Bingrui Wang, PhD** | University of Pittsburgh
*Mentor: Ian Sigal, PhD*

Blindness in glaucoma is caused by damage to axons that carry visual information to the brain. Damage often starts in the back of the eye and is due to high eye pressure, which mechanically deforms axons. However, the link between axon deformation and long-term damage is unclear. Using animal models, researchers will investigate axon deformation and its link to damage to understand glaucoma's causes.

## Why Certain Retina Ganglion Cells Stay Strong in Glaucoma

**Mengya Zhao, PhD** | University of California, San Francisco
*Mentor: Xin Duan, PhD*

This project focuses on understanding the mechanisms underlying neuronal loss in glaucoma, which can lead to irreversible blindness. This disease variably impacts many eye neurons. Using a combination of cutting-edge techniques, researchers will investigate why certain neurons are more resilient than others. This work could unlock new treatments, offering a breakthrough in glaucoma therapy and eye care.

# Understanding What Causes Glaucoma

Glaucoma threatens sight by damaging the optic nerve, primarily due to chronic elevated intraocular pressure (IOP) from improper fluid drainage. National Glaucoma Research funds studies on the genetics of glaucoma, including racial and ethnic disparities in its incidence, and more sensitive methods for detecting its onset. Scientists are also developing new research models to better understand glaucoma and create new therapies.

## The Genetics of Glaucoma in Individuals of Caucasian and African Ancestry

**Michael Hauser, PhD** | Duke University

Researchers will examine the expression levels of glaucoma-associated genes in individual retinal cells and the effects of different versions of these genes. The studies will yield basic information that will advance understanding and could lead to development of new glaucoma treatments. Most crucial, the team will follow up on new findings in African Americans, a group disproportionately affected by glaucoma.

## Defining the Role of a New Protein Target in Fluid Buildup in Glaucoma

**Rupalatha Maddala, PhD** | Duke University School of Medicine
*Co-Principal Investigators: Pratap Challa, MD & Vasantha Rao, PhD*

In this project, researchers will assess the role of septins, proteins that are implicated in glaucoma, in fluid drainage from the eye. They will focus on the trabecular meshwork, which is where fluid drains from the eye, and how septins affect the function of this area. The findings will highlight specific features of septins and their role in fluid pressure in the eye that could be targets in glaucoma treatment.

## Human Stem Cell Modeling of the *APBB2* Risk Variant for Glaucoma

**Jason Meyer, PhD** | Indiana University School of Medicine in Indianapolis

Recently, a variant in a gene, *APBB2*, was identified as significantly associated with glaucoma in African Americans, offering a novel opportunity to explore the degeneration of retinal ganglion cells (RGCs) associated with the increased risk. Researchers will focus on using adult stem cells and CRISPR/Cas9 gene editing as an in vitro model to study the effects of this gene variant on RGCs and how it may lead to glaucomatous neurodegeneration.

## Understanding Alterations in an Early Experimental Glaucoma Model

**Hongli Yang, PhD** | Good Samaritan Foundation, Legacy Health System

*Co-Principal Investigator: Priya Chaudhary, PhD*

The goal of this project is to identify the cellular and molecular alterations underlying structural change in an experimental model. Overall, this project will inform and enhance the interpretation of human optical coherence tomography imaging, advance our understanding of pathophysiologic mechanisms in glaucoma, and provide guidance to improve therapeutic options before damage from glaucoma becomes permanent and untreatable.

## Understanding How Variants in LOXL1 Affect Pseudoexfoliation Glaucoma Risk

**Hannah Youngblood, PhD** | Georgia Institute of Technology

*Mentor: Raquel Lieberman, PhD*

Genetic variants in the LOXL1 gene can alter risk for pseudoexfoliation glaucoma (XFG), a blinding disease that affects more than 10 million people. This project seeks to determine how these variants alter the structure and function of the LOXL1 protein. Successful completion of this project will provide a better understanding of how LOXL1 variants contribute to XFG and provide the groundwork for therapeutic development.

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